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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,852	09/22/2000	Per Johan Lundberg	1103326-0686	1116

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PATENT DEPARTMENT
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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,852	LUNDBERG ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-18,20 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-18,20 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/06/06*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 3/14/06
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 6-8, 12-18, 20 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Hodges et al. US 5,225,202.

Nara teaches a controlled release composition comprising a drug-containing core coated with a coating composition containing a water-insoluble substance and a swellable polymer (abstract, column1, lines 50-63). Drugs include omeprazole and lansoprazole, are mixed with excipient, such as sucrose or calcium phosphate (osmotic agent); binder; disintegrant, such as, sodium crosslinked carboxymethylcellulose or low-substitutional hydroxypropyl cellulose (swelling agent); and lubricant, including talc (alkaline additive) (column 3, lines 59-61; column 5, lines 36-52). Core can be in the

form of granule, fine granule, or inert carrier particles include sucrose (column 5, lines 30-35, and 60-65). The water-insoluble substance contained in the coating composition includes ethyl cellulose, cellulose acetate, and Eudragit RS (column 4, lines 5-25; and column 6, lines 15-25). The coating composition further comprises talc (modifying agent) (column 6, lines 50-55; and example 3). The examples show the weight of coating composition is about 20-30% to the core. The coated core can be prepared in tablet or capsule form for oral administration (column 6, lines 56-65; and claim 7).

It is noted that Nara does not explicitly teach the weight ratio of the modifying agent to water-insoluble substance, as well as the amount of the alkaline additive and swelling agent in the core. However, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, it would have been obvious to one of ordinary skill in the art to, by routine experimentation determine suitable amount of talc in the core composition as well as in the coating composition, because Nara teaches the release rate of the active ingredient is mainly in the small and large intestine without an enteric coating, while the release rate of the active ingredient is very limited in the stomach (column 1, lines 53-55; and column 7, lines 25-31), and because Nara teaches a coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without

enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Nara does not explicitly teach the amount of alkaline additive present in the core.

Hodges teaches a controlled release pellet comprising acid labile drug in the core, and one or more buffering agents (alkaline additives) (see abstract, and column 3, lines 1-4; lines 15-19). Buffering agents present in the core in an amount ranging from about 1 to about 20% (column 3, lines 34-36). Thus, it would have been obvious to one of ordinary skill in the art to use alkaline additive in an amount taught by Hodges to obtain a stable acid labile composition, because Hodges teaches using buffering agent in an amount of about 1 to about 20% to aid in minimizing drug degradation in the core due to acid ingress in low pH environments (column 3, lines 6-9), and because Nara teaches a composition with low toxicity and can be safely used in mammals.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Hodges et al. and Zentner US 4,795,644 or Lundberg et al. 6,013,281.

Nara and Hodges are relied upon for the reason stated above. Hodges is silent as to the claimed alkaline agent.

Zentner teaches pH modifying agent includes sodium mono- or di-phosphate (column 8, lines 3-15).

Lundberg teaches alkaline reacting compound includes arginine (column 6, lines 50-55). Thus, it would have been obvious to one of ordinary skill in the art to modify the

compositions of Nara and Hodges using sodium mono- or di-phosphate and arginine compound as an alkaline agent, because the references teach suitable composition for the same active agent, namely, omeprazole.

Claims 4, 5 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Hodges et al., and Cotton et al. WO 98/54171.

Nara and Hodges are relied upon for the reason stated above. Nara is deficient in the fact that Nara does not specifically teach magnesium salt of omeprazole.

Cotton teaches novel form of S-enantiomer of omeprazole, including S-omeprazole, and more specifically, magnesium salt of S-omeprazole trihydrate (hereafter, the compound) (see abstract, and page 1, lines 4-10). Cotton also teaches the compound is formulated into oral dosage form, *e.g.*, capsule, tablet, and the like (page 6, lines 15-30). The formulation is effective as a gastric acid secretion inhibitor and is useful as an anti-ulcer agent (page 6, lines 1-14).

Cotton does not explicitly teaches the compound having a crystallinity of more than 70%, however, Cotton teaches that the compound of his invention is highly crystalline, *i.e.*, having a higher crystallinity than any other form of magnesium salt of S-omeprazole in the prior art (page 3, lines 24 through page 4, lines 1-7). Therefore, the burden is shifted to applicant to show the compound taught by Cotton does not have the crystallinity being claimed. It is also noted that Cotton teaches the trihydrate form, *e.g.*, magnesium salt of S-omeprazole "trihydrate". However, applicant claims recite a

generic form of magnesium salt of S-omeprazole with the transitional phrase "comprising of" permits any other form, including "trihydrate" taught by Cotton. Thus, it would have been obvious for one of ordinary skill in the art to modify the controlled release composition comprising a drug-containing core coated with a *non-enteric* coating composition using the magnesium salt of S-omeprazole trihydrate in view of the teaching of Cotton, because Cotton teaches the compound of his invention is more stable, easier to handle and store, easier to synthesize in a reproducible manner, because Cotton teaches the compound is most preferred in oral administration formulation, because Nara teaches a non-enteric coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Response to Arguments

Applicant's arguments filed 12/15/05 have been fully considered but they are not persuasive.

Applicant argues that Hodges does not recognize the problem solved by the claimed invention which is directed to oral dosage forms which are not enteric-coated. In response to applicant's arguments against Hodges individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that it is indisputable that Hodges teaches away from both Nara and the claimed invention, because the pharmaceutical formulations disclosed by Hodges have an enteric coating which protects the acid-labile active ingredient from the acid gastric fluid during its passage through the stomach. Accordingly, the person of ordinary skill in the art who is interested in formulating a dosage form without an enteric coating layer, would have had no motivation to consider Hodges alone or in combination with Nara. In response to applicant's argument that there is no motivation to combine Nara and Hodges, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Hodges is cited solely for the teaching that buffering agent can be used in the core in an amount effective to minimize drug degradation in the core. It is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Accordingly, it would have been obvious to one of ordinary skill in the art to combine the teachings of Nara and Hodges to obtain the claimed invention, because Nara does teach the use of the claimed alkaline additives (such as talc). Hodges is relying on for the teaching of the amount of alkaline additives.

Applicant argues that applicant relies on the complete absence of any disclosure, suggestion or recognition by Nara of the necessity of including a sufficiently high amount of an alkalize additive in a core. Specifically, Nara states that the dosage form may *optionally* contain talc present in a formulation at a 5% concentration. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Nara is cited in view of Hodges for the further teaching of using additives in the core, such as alkalize additive in an amount effective to prevent degradation of the active agent in the core (column 3, lines 6-9). Furthermore, it does not appear that talc is optionally used. At column 5, lines 35-39 and 51-52, Nara teaches that the core is mixed with appropriate excipient, binder, disintegrant, and lubricant, wherein lubricant includes talc.

Applicant argues that the coating composition of Nara contains a hydrophilic substance and a swellable agent, both of which are excluded from the semipermeable membrane of the claimed invention in view of the use of the transitional phrase "consists of". However, a review of Nara showing the coating composition of Nara may

and may *not* comprise the hydrophilic substance in view of the teaching at column 5, lines 14-18, Nara teaches the coating composition may comprise hydrophilic in an amount ranging from 0%. Regarding to the swellable agent, it is noted that the swellable agent is also present at a very small amount, from *about* 1%. Although the transitional phrase "consisting of" excludes any ingredient not specified in the claim, the present of impurities ordinarily associated therewith is permitted. Norian Corp. v. Stryker Corp., 363 F.3d 1321, 1331-32, 70 USPQ2d 1508, 1516 (Fed. Cir. 2004). Regardless, the burden is shifted to applicant to establish that the present of swellable agent in a small amount would have a detrimental effect upon the desirability of forming a delayed release oral dosage form. Applicant's attention is called to column 7, lines 33-46, Nara teaches the advantageous results are sustained drug release over a long period of time (12-24 hours in vitro), maintain a constant drug concentration in plasma, and high biological availability.

Applicant argues that Cotton does not over come the deficiencies of Nara and Hodges. In response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Cotton is cited solely for the teaching of magnesium salt of S-omeprazole trihydrate effective as a gastric acid secretion inhibitor and is useful as an anti-ulcer agent (page 6, lines 1-14).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-R from 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached at (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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